K071781

DEC 1 9 2007

GTI DIAGNOSTICS
Good science starts with people.

IN USA 800 . 233 . 1843
TEL 262 . 754 . 1000
FAX 262 . 754 . 9831
EMAIL gti@gtidiagnostics.com
WWW gtidiagnostics.com

20925 Crossroads Circle, Suite 200
Waukesha, WI 53186 USA

510(k) Summary

I. Submitter:

Owner's Name:	Genetic Testing Institute, Inc. (GTI)
Address:	20925 Crossroads Circle, Waukesha, WI 53186
Phone:	262.754.1000
Fax:	262.754.9831
Name of Contact Person:	Suzette C. Chance, Ph.D.
Date Summary Prepared:	June 15, 2007

II. Name of Device:

Device Name: PF4 IgG™ Solid Phase ELISA

Proprietary Name: PF4 IgG™

Classification Name: Platelet Factor 4 Radioimmunassy

Product Code: LCO

III. Name of predicate device for claiming equivalence

GTI-PF4 ENHANCED® (K053559)

IV. Description of Device:

The PF4 IgG™ assay is an Enzyme Linked Immunosorbent Assay (ELISA). The PF4 IgG™ ELISA is intended to detect IgG antibodies in human serum that react with Platelet Factor 4 (PF4) when it is complexed to heparin or other polyanionic compounds. The PF4 IgG™ kit contains all of the reagents necessary to perform the assay.

Antibodies that react with PF4 when it is complexed to heparin are found in some patients undergoing heparin therapy. The presence of these antibodies has been shown to be associated with heparin induced thrombocytopenia Type II (Type II HIT). Heparin Induced Thrombocytopenia (HIT) is an adverse reaction that can occur in patients that are undergoing heparin therapy. HIT occurs in up to 3% of patients that are receiving heparin and can result from treatment with either low molecular weight heparin (LMWH) or unfractionated heparin (UFH). HIT is usually associated with thrombocytopenia and in some cases the more severe complications of arterial or venous thrombosis. The pathophysiology of HIT is linked to the formation of antibodies which are specific for epitopes formed when heparin binds to PF4. These antibodies can subsequently bind to platelets via the FcγRIIa receptor resulting in platelet activation.

It has been previously shown that antibodies which bind to PF4/heparin complexes also bind to PF4 when it is complexed with other polyanionic compounds such as polyvinyl sulfonate (PVS). In the PF4 IgG™ assay, a complex of PF4/PVS, which has been immobilized in the microwells serve as a target for the binding of antibodies associated with Type II HIT.

In the PF4 IgG™ assay, patient serum is first diluted (1:4), with the specimen diluent provided in the kit. The diluted sample is then added to microwells to which Platelet Factor 4 (PF4) complexed to polyvinyl sulfonate (PVS) has been immobilized. The sample is then incubated for 30 minutes at 37°C. If an antibody which recognizes a site on PF4/PVS complex is present in the patient sample, binding will occur. Following this incubation, a wash step then removes any unbound antibodies. A goat anti-human IgG – alkaline phosphatase conjugate is then added to the wells. The conjugate is incubated for 30 minutes at 37°C. Following this incubation, a wash step then removes any unbound conjugate. The alkaline phosphate substrate, p-nitrophenyl phosphate (pNPP) is then added to the microwells. After a 30 minute incubation at room temperature (22 – 25°C), the reaction is stopped by addition of the stopping solution (3 M sodium hydroxide). The optical density of the color that develops is measured in a spectrophotometer at 405 or 410 nm using a reference wavelength of 490 nm.

V. Intended Use

PF4 IgG™ is a qualitative solid phase enzyme linked immunosorbent assay (ELISA) designed to detect antibodies reactive with Platelet Factor 4 (PF4) when it is complexed to polyanionic compounds such as polyvinyl sulfonate (PVS). These antibodies are found in some patients undergoing heparin therapy.

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VI. Support of substantial equivalence based on comparison of features, characteristics and components to the predicate device:

A comparison of the features and characteristics of the two devices can be summarized as follows:

	PF4 ENHANCED®	PF4 IgG™
Intended Use	PF4 ENHANCED® is a qualitative solid phase enzyme linked immunosorbent assay (ELISA) designed to detect antibodies reactive with Platelet Factor 4 (PF4) when it is complexed to polyanionic compounds such as polyvinyl sulfonate (PVS). These antibodies are found in some patients undergoing heparin therapy.	PF4 IgG™ is a qualitative solid phase enzyme linked immunosorbent assay (ELISA) designed to detect IgG antibodies reactive with Platelet Factor 4 (PF4) when it is complexed to polyanionic compounds such as polyvinyl sulfonate (PVS). These antibodies are found in some patients undergoing heparin therapy.
Indications for Use	PF4 ENHANCED® is designed as a solid phase enzyme-linked immunosorbent assay (ELISA). This product is intended to be used as an in vitro diagnostic kit by hematology, coagulation, or other pathology laboratories to assist in screening patient samples for the presence of heparin-associated antibodies commonly found in patients with heparin-induced thrombocytopenia or thrombosis.	PF4 IgG™ is designed as a solid phase enzyme-linked immunosorbent assay (ELISA). This product is intended to be used as an in vitro diagnostic kit by hematology, coagulation, or other pathology laboratories to assist in screening patient samples for the presence of heparin-associated antibodies commonly found in patients with heparin-induced thrombocytopenia or thrombosis.
Technology	ELISA with a colorimetric measurement system	ELISA with a colorimetric measurement system

Reportable Results	Qualitative assay; results are reported as positive or negative	Qualitative assay; results are reported as positive or negative
Packaging Configuration	13 and 45 Test kits	13 and 45 Test kits
Reagents:		
Microwell strips	Immobilized PF4/PVS Complex	Immobilized PF4/PVS Complex
Concentrated Wash Solution	10X Tris Buffer, NaCl, Tween 20, 1% NaN_3	10X Tris Buffer, NaCl, Tween 20, 1% NaN_3
Specimen Diluent	Phosphate Buffered Saline, 0.05% NaN_3	Phosphate Buffered Saline, 0.05% NaN_3
Substrate Buffer	Diethanolamine and magnesium chloride, 0.02% NaN_3	Diethanolamine and magnesium chloride, 0.02% NaN_3
Substrate	PNPP (crystalline powder)	PNPP (crystalline powder)
Stopping Solution	3 M NaOH	3 M NaOH
Positive Serum Control	Human serum containing Bovine Albumin and 0.1% NaN_3	Human serum containing Bovine Albumin and 0.1% NaN_3
Negative Serum Control	Human serum containing 0.1% NaN_3	Human serum containing 0.1% NaN_3
Conjugate	Goat anti-human Ig G+A+M conjugated to alkaline phosphatase enzyme	Goat anti-human Ig G conjugated to alkaline phosphatase enzyme

The similarities between these two products can be summarized as follows:

- Both PF4 IgG™ and PF4 ENHANCED® have similar intended uses and the same indications for use
- PF4 IgG™ and PF4 ENHANCED® use the same technology (ELISA) and assay steps
- PF4 IgG™ and PF4 ENHANCED® have identical reagents with the exception of the conjugate used for antibody detection

The difference between the two products can be summarized as follows:

The PF4 ENHANCED® kit utilizes a conjugate that detects bound human IgG, IgA, and/or IgM antibodies (goat anti-human IgG+A+M conjugated to alkaline phosphatase). The PF4 IgG™ kit utilizes a conjugate that detects bound human IgG (goat anti-human IgG conjugated to alkaline phosphatase).

VI. Support of substantial equivalence with performance data:

The details of each of the following studies are covered in Section 7: Performance Data of this 510(k). Only a brief summary of these studies is provided in this section.

Assay Precision

Description of Study

Three samples of varying antibody concentrations were prepared by diluting a patient sample (sera) containing a high level of an anti-PF4/heparin antibody into a pool of normal serum containing no PF4/heparin antibody. This sample was diluted to obtain 3 separate samples that had low positive reactivity (approximately 0.5 O.D. or 0.1 O.D. units above the cutoff), medium positive reactivity, and high positive reactivity. In addition to these samples, the positive and negative controls provided in the kit were used for this study. The positive control consists of a human serum containing a PF4/heparin IgG antibody, whereas the negative control consists of a sera sample containing no PF4/heparin antibody.

Each sample or control was tested in duplicate in the PF4 IgG™ assay in 10 separate assays.

Results and Analysis

To obtain imprecision of the O.D. values, the data were analyzed by ANOVA according to CLSI Document EP-5A2, Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline. In addition, the reportable result (positive or negative) was analyzed for agreement within and between runs according to CLSI Document

EP 12-A Vol. 22, No 14, User Protocol for Evaluation of Qualitative Test Performance; Approved Guideline.

The calculations of imprecision for the O.D. values showed that the assay demonstrated ≤10% cv total imprecision for samples of all levels of PF4/PVS antibody reactivity. In addition, the correct reportable result was obtained for each result of each assay. There was 100% agreement between all reportable results (within-run and between-run) for each sample tested.

Conclusions

The PF4 IgG™ assay showed acceptable assay imprecision of the O.D. values as well as the reportable results.

Normal Range and Assay Cutoff

Description of Study:

One hundred and twenty serum samples were obtained from normal healthy individuals and were tested (in duplicate) in the PF4 IgG™ and the PF4 ENHANCED® assays. The mean of the duplicates was obtained for each sample tested and the results were analyzed for normality of the distribution of the O.D. values.

Results and Analysis:

The results showed that neither set of data were normally distributed. A non-parametric analysis was used to determine the normal range for each assay. The normal ranges were calculated to be 0.142 - 0.352 for PF4 IgG™ and 0.332 - 0.407 for PF4 ENHANCED®. The calculations were based on a non-parametric 95% reference interval with a 90% confidence. The cutoff for the assays was then taken to be the upper end of the normal range (0.352 for PF4 IgG™ and 0.407 for PF4 ENHANCED®). Calculations for the normal range were performed by GTI's Manager of Clinical and Scientific Affairs (Melissa Pressman, Ph.D.), using the Med Calc software program.

Conclusions:

While statistically different, the upper end of the normal ranges for the PF4 ENHANCED® and the PF4 IgG™ assays were not significantly different. Therefore, the cutoff of ≥0.400 was confirmed for the PF4 ENHANCED® assay and established for the PF4 IgG™ assay.

Comparison of Methods Study

Accuracy was demonstrated by a study in which PF4 IgG™ was compared to both the PF4 ENHANCED® assay and the Serotonin Release Assay (SRA). The following provides a

description of the study, the results, and conclusions. This study was conducted as an internal study at GTI.

Description of Study:

The samples used in the method comparison study consisted of a set of 229 different sera obtained from the BloodCenter of Wisconsin (BCW). Each sample was provided in a single aliquot and was stored frozen at -80°C until the time it was tested. These samples were obtained from patients receiving heparin treatment and were originally tested by the BCW for the presence of PF4/heparin antibodies by the SRA. The SRA is an "in house assay" that detects the presence of antibodies in serum that are capable of activating platelets. The SRA is considered to be the gold standard for testing for antibodies that can cause HIT.

Samples were tested in duplicate in the PF4 IgG™ and PF4 ENHANCED® assays at GTI. The mean of the O.D. values for each sample was obtained. Results were considered to be positive in the PF4 IgG™ and PF4 ENHANCED® assays if the mean of the O.D. value was ≥0.400. Results from the SRA were based on the data provided by the BCW.

Results and Analysis:

Analysis of the data was performed using 2x2 tables. The PF4 IgG™ assay results were compared to the PF4 ENHANCED® and the SRA. In addition, the PF4 ENHANCED® assay results were compared to those of the SRA. The calculations for co-positivity, co-negativity, and % agreement for each comparison are shown in the table below.

	PF4 IgG™ Versus SRA	PF4 ENHANCED® Versus SRA	PF4 IgG™ versus PF4 ENHANCED®
Sensitivity (Co-Positivity)	100%	100%	74%
95% Confidence Interval	84.5 – 100.0%	84.5 – 100.0%	61.0 – 83.4%
Specificity (Co-negativity)	90%	83%	100%
95% Confidence Interval	85.1 – 93.3%	77.0 – 87.2%	97.8 – 100.0%
% Agreement	91%	84%	93%

Conclusions:

The PF4 IgG™ assay showed excellent specificity (co-negativity), and agreement with the predicate device (PF4 ENHANCED®). Although the sensitivity (co-positivity) of the PF4 IgG™ assay compared to the predicate device was only 74%, some of these discordant results could be explained by the fact that some of these samples may contain only IgM and/or IgA antibodies. However, more importantly, the PF4 IgG™ assay showed an improved specificity (co-negativity) over the PF4 ENHANCED® assay when compared to

the Serotonin Release Assay (SRA). The SRA is considered to be the gold standard for detection of antibodies that result in HIT.

Stability

No additional stability studies were conducted on the PF4 IgG™ kit since this kit consists of reagents that are used in other kits manufactured by GTI for which stability has already been demonstrated. All of the components of PF4 IgG™ kit with the exception of the anti-human IgG conjugate are identical to those of the PF4 ENHANCED® for which stability of each component has already been established. The anti-human IgG conjugate used in the PF4 IgG™ kit is used in other GTI kits for which stability has also been established. These kits have previously cleared by FDA (GTI QuikScreen®; BK950005 and GTI BScreen®; BK 990043). The expiration of the PF4 IgG™ kit is determined by the expiration dating of the component with the least expiration date.

VIII. Conclusion:

Based on comparison with the predicate device, (PF4 ENHANCED®), these data demonstrate that PF4 IgG™ performs comparable to the predicate device and the PF4 IgG™ kit does not present new issues of safety and effectiveness.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

DEC 1 9 2007

Genetic Testing Institute
C/O Suzette C. Chance
20925 Crossroads Circle
Suite 200
Waukesha, Wisconsin 53186-4054

Re: k071781
Trade/Device Name: PF4 IGG
Regulation Number: 21 CFR 864.7695
Regulation Name: Platelet Factor 4 Radioimmunassay
Regulatory Class: Class II
Product Code: LCO
Dated: June 15, 2007
Received: July 2, 2007

Dear Ms. Chance:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

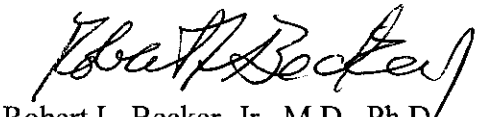
If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820). This letter

will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please contact the Office of In Vitro Diagnostic Device Evaluation and Safety at (240) 276-0450. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). For questions regarding postmarket surveillance, please contact CDRH's Office of Surveillance and Biometric's (OSB's) Division of Postmarket Surveillance at (240) 276-3474. For questions regarding the reporting of device adverse events (Medical Device Reporting (MDR)), please contact the Division of Surveillance Systems at (240) 276-3464. You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (240) 276-3150 or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,



Robert L. Becker, Jr., M.D., Ph.D.
Director
Division of Immunology and Hematology
Office of *In Vitro* Diagnostic Device Evaluation
and Safety
Center for Devices and Radiological Health

Enclosure

Indications for Use

510(k) Number (if known): K071781

Device Name: PF4 IgG™

Indications For Use: PF4 IgG™ is a qualitative screening assay for the detection of heparin associated IgG antibodies in human serum. The presence of heparin associated antibodies are commonly found in patients with Heparin Induced Thrombocytopenia (HIT).

Prescription Use X AND/OR Over-The-Counter Use _____
(Part 21 CFR 801 Subpart D) (21 CFR 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of In Vitro Diagnostic Devices (OIVD)

Division Sign-Off

Office of In Vitro Diagnostic Device Evaluation and Safety

510(k) K071781